DETAILED ACTION

Claims 1-8, 16 and 18-23 are pending in this application.

Claim Objections

Claim 7 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a bacterial infection due to *Staphylococcus aureus*, does not reasonably provide enablement for a method of treating bacterial infection generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination

that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to 'a method of treating a bacterial infection' - which covers all types of bacteria and the infections due to them, without any particular cause, that are known to exist and those that may be discovered in the future, for which there is no enablement provided. There are no test procedures/assays provided to test the pharmaceutical or therapeutic activity of the compounds or efficacy in treating 'any disease or disorder due to bacterial infection' in general and none of the compounds have been tested to cover the effectiveness for all types of infections due to the bacterial and diseases or disorders due to bacterial infections generally. The test procedures provided in the specification in page 20 are drawn to general procedure to test the antimicrobial efficacy of the compounds, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to treatment of **all** types of bacterial infections and diseases or disorders embraced the instant claims. One of ordinary skill would not know to extrapolate this test data to method of treating diseases or disorders generally. Further, there is no reasonable basis for assuming that all the compounds embraced by the claims will share the same physiological properties and will be useful generally against any type of disease because there is no basis in the prior art for assuming the same.

Also see MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area. It is inconceivable as to how the claimed compounds can treat all types of diseases. For example, there is no known common therapeutic mechanism for all types

of diseases generally. For example, there are more than 400 distinct viruses that infect humans producing a wide range of diseases. Bacterial infections are caused by the presence and growth of microorganisms that damage host tissue. The extent of infection is generally determined by how many organisms are present and the toxins they release. Infectious diseases are human illnesses caused by viruses, bacteria, parasites, fungi and other microbes. They may be spread by direct contact with an infected person or animal, by ingesting contaminated food or water, by insects like mosquitoes or ticks (disease vectors), or by contact with contaminated surroundings like animal droppings or even contaminated air. Bacteria can cause a range of different problems in different parts of the body. Applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of preventing solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable". Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc.

No compound has ever been found that can treat bacterial infections generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Nearly all drugs for treating infections are effective against

only a limited group of disorders. Therefore, a compound effective against disorders of the neuronal system generally would be a revolutionary exception. It is well established that an enablement rejection is proper when the scope of enablement is not reasonably correlated to the scope of the claims. (*In re Vaeck*, 20 USPQ2d 1439, 1444 (CAFC 1991); *In re Ferens*, 163 USPQ 609).

It is inconceivable as to how the claimed compounds can treat all types of bacterial infections for which applicants provide no competent evidence. For example, there is no common mechanism by which all bacterial infectious conditions arise. Accordingly, treatments for these diseases are normally tailored to the particular type of microorganism or infection present and there is no 'magic bullet' against infections in general.

There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) due to such infections. There is no evidence in the record which demonstrates that the screening test relied upon are recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'therapeutic treatment' of all types of bacterial infections. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse* et al., 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility and not "warranting further study"). The evidence presented in this case does not show such utilities, but only warrants further study.

(Only a few of the references pertinent to the claims are discussed here to make the point of an insufficient disclosure and to indicate that the scope of the claim does not meet the enablement requirement).

1) The nature of the invention: The use of the compound in 'a method of treating bacterial infections' in general.

2) The state of the prior art: There are no known compounds of similar structure that have been demonstrated to be effective against **all** types of bacteria generally.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, 'the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved'. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The online edition of The Merck Manual of Diagnosis and Therapy indicates that 'when bacteremia produces changes in circulation such that tissue perfusion is critically reduced, septic shock ensues' and further provides that 'the pathogenesis of septic shock is not completely understood'.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: The specification provides tests to determine the activity of the compounds in relation to specific organisms.

6) The breadth of the claims: The instant claims embrace the treatment of 'a disease or disorder due to any type of bacterial infection'.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and

"predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 16 and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In the claims, it is recited that "A compound.... **and** pharmaceutically acceptable salt**s** thereof", which is unclear because it is not clear if 'a compound or a salt thereof' is claimed **or** 'a **mixture** of a compound and the salt' is claimed. Replacing with -- A compound..... ~~and~~ or a pharmaceutically acceptable ~~salts~~ salt thereof -- would overcome the rejection.
2. In claim 3, it is recited that "R^5 and R^6 are as defined in formula I" (see line 6). The claim, however, is an independent claim. An independent claim must contain all limitations within the claim or should refer to another claim in which the limitations are recited.

3. In claim 4, it is recited that "R^5 and R^6 are as defined in formula I" (see line 6). The claim, however, is an independent claim. An independent claim must contain all limitations within the claim or should refer to another claim in which the limitations are recited.
4. In claim 5, it is recited that "R^5 and R^6 are as defined in formula I" (see line 6). The claim, however, is an independent claim. An independent claim must contain all limitations within the claim or should refer to another claim in which the limitations are recited.
5. Claim 7, drawn to intermediate compounds of formula XI and XII, refers to claims 1 and 2 for the definitions of the variables. Claims 1 and 2, however, are drawn to compounds of formula I and I', which are structurally different. It is suggested that claim 7 be rewritten as an independent claim with the definitions of all variables.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 16 and 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burri et al., WO 02/10156. The reference teaches substituted benzofuran compounds that are structurally analogous to instantly claimed compounds. See the compounds of formula I disclosed in page 2 and the corresponding species in pages 4-6. The compounds are taught to be useful as antibacterial agents, see the abstract. For example, the reference teaches the compound: 5,6-[dimethoxy-2-(indol-1-ylmethyl)benzofuran-4-ylmethyl]pyrimidine-2,4-diamine (see page 6, line 16). The instant compounds differ from the reference disclosed compound by having the indolyl group attached via a position different from the reference compounds, i.e., at the 3-position as compared to the reference compound which is attached through the 1-position. Therefore, the instantly claimed compounds are positional isomers of the reference compounds. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare the instantly claimed compounds because they are positional isomers of the reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such isomeric compounds are suggestive of one another and would be expected to share similar properties and therefore, the same use as taught for the reference compounds, i.e., as antibacterial agents. It has been held that a compound, which is structurally isomeric with a compound of prior art is prima facie obvious absent unexpected results. *In re Finley*, 81 USPQ 383 (CCPA 1949); *In re Norris*, 84 USPQ 458 (CCPA 1950); *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Receipt is acknowledged of the Information Disclosure Statement filed on January 10, 2006 and copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

June 25, 2008